

U.S.S.N. 09/235,875

Filed: January 22, 1999

**AMENDMENT AND RESPONSE TO OFFICE ACTION****Remarks**

Applicants appreciate the withdrawal of the rejection of the claims over the prior art and withdrawal of the rejections under obvious double patenting and 35 U.S.C. 112, first paragraph in the Office Action mailed February 10, 2006.

As discussed in the interview held March 8, 2006 with the Examiner, Dr. Peoples and the undersigned, the art cited in the Office Action mailed February 10, 2006 describes production of 3-hydroxyhexanoate containing polymers by the beta oxidation pathway by providing substrates of C6 or longer fatty acids. In contrast to the cited art, the present application discloses genetically engineering bacteria to produce of 3-hydroxyhexanoate from butyryl-CoA plus acetyl-CoA.

**Claim Objections**

The claims have been amended as suggested by the Examiner to recite that the bacteria can use butyrate and butanol as substrates. Support for this amendment can be found in the specification at least at page 5, line 10. The claims have also been amended to overcome the formal objections raised in the Office Action mailed February 10, 2006 and pursuant to the interview held March 8, 2006 with the Examiner, Dr. Peoples and the undersigned. Applicants greatly appreciate the interview. It is our understanding that these amendments place the claims in condition for allowance. The claims have been amended for consistency to refer to "3" instead of "beta" or " $\beta$ ." Claim 20 has been amended to refer to the same enzyme as recited in claim 10 as requested by the Examiner. Claim 17 has also been amended as requested by the Examiner to reduce redundancy of the recited enzymes. Claim 10 has been amended to depend

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upon claim 19 for consistency. Claims 10, 16, 17 and 18 have been amended to correct verb tense. Claims 7 and 14 have been amended to recite "bacterium" instead of "bacteria." New claims 35-39 have been added. Support for these claims can be found at least at original claims 22-26 and at page 6, lines 4-8, page 14, lines 5-14, Figure 5 and page 12, lines 1-15.

**Rejection Under 35 U.S.C. § 102**

Claims 1, 7, 16 and 18-21 were rejected under 35 U.S.C. § 102(b) as being anticipated by Fukui, et al., *J. of Bacteriol.* 179:4821-4830 (1997) ("Fukui"). Applicants respectfully traverse this rejection.

Fukui discloses production of poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) by the beta oxidation pathway by providing substrates of C6 or longer fatty acids, specifically hexanoate and octanoate. As discussed with the Examiner the claims of the present application are drawn to production of 3-hydroxyhexanoate from butyryl-CoA plus acetyl-CoA, which is not disclosed or suggested by Fukui. Therefore, Fukui does not anticipate the claims of the present application.

**Rejections Under 35 U.S.C. § 103**

Applicants respectfully traverse these rejections.

(i) Claims 1, 6-7, 16 and 18-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Fukui, in view of U.S. Patent No. 5,470,727 to Macharenas, et al. ("Macharenas") and further in view of Schubert, et al., *J. of Bacteriology* 1998, Vol. 170, No. 12, p. 5837-5847 ("Schubert").

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As discussed above, the claims are drawn to production of 3-hydroxyhexanoate from butyryl-CoA and acetyl-CoA, which is not disclosed or suggested by Fukui.

Macharenas and/or Schubert do not make up for this deficiency since neither reference discloses or suggests production of 3-hydroxyhexanoate from butyryl-CoA and acetyl-CoA. Therefore, the claims are not obvious.

(ii) Claims 1, 7, 10 and 18-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Timm, et al., *Applied and Environmental Microbiology*, 56(11):3360-3367 (1990) ("Timm"), in view of Fukui and further in view of Hoffmann, et al., *FEMS Microbiology Letters* 184:253-259 (2000) ("Hoffmann").

Timm discloses production of 3-hydroxyhexanoate containing polymers when octanoate is given as substrate (see page 3366, column 1, first full paragraph). Timm does not disclose or suggest production of 3-hydroxyhexanoate from butyryl-CoA and acetyl-CoA. Fukui and Hoffmann do not make up for this deficiency. Fukui also discloses production of 3-hydroxyhexanoate containing polymers from octanoate or hexanoate, not butyryl-CoA and acetyl-CoA. Hoffmann discloses production of PHAs from gluconate, not butyryl-CoA and acetyl-CoA. Timm, Fukui and Hoffmann do not disclose or suggest using butyryl-CoA and acetyl-CoA as substrates for production of polymers containing 3-hydroxyhexanoate. Therefore, the claims are not obvious.

(iii) Claims 1, 7, 14 and 16-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Schubert, in view of Fukui and further in view of Boynton, et al., *J. of*

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*Bacteriology* 178(11):3015-3024 (1996) ("Boynton") and Feigenbaum, et al., *PNAS* 74(2):492-495 (1977) ("Feigenbaum").

Schubert discloses production of poly- $\beta$ -hydroxybutyric acid (PHB) in *E. coli*. Schubert does not disclose or suggest genetically engineering bacteria to produce 3-hydroxyhexanoate containing polymers from butyryl-CoA and acetyl-CoA. Fukui, Boynton and Feigenbaum do not make up for this deficiency. As discussed above Fukui discloses use of hexanoate or octanoate as substrates for production of 3-hydroxyhexanoate containing polymers. Feigenbaum discloses isolation of a multi-enzyme complex of fatty acid oxidation from *E. coli*. Boynton discloses cloning of  $\beta$ -hydroxybutyryl-CoA dehydrogenase and butyryl-CoA dehydrogenase from *C. acetobutylicum*. Feigenbaum and Boynton do not disclose or suggest genetically engineering bacteria to produce 3-hydroxyhexanoate containing polymers from butyryl-CoA and acetyl-CoA. Clearly it would not be obvious to one of skill in the art how to genetically engineering bacteria to produce 3-hydroxyhexanoate containing polymers from butyryl-CoA and acetyl-CoA based on the cited art. Therefore, the claims are not obvious.

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Allowance of claims 1, 6-7, 10, 14 and 16-21 is respectfully solicited.

Respectfully submitted,

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